

# Risk Factors and Incidence of Venous Thromboembolism after Total Knee Replacement

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## Abstract

Patients undergoing total knee arthroplasty can be at risk in developing venous thromboembolism. The etiology of venous thromboembolism after a total knee arthroplasty is multifactorial. The aim of this study is to present the risk factors and the incidence of venous thromboembolism among the 276 patients, who underwent a total of 348 knee arthroplasty treatments in the King Abdulaziz University Hospital. Three hundred (86.2%) patients had undergone unilateral total knee arthroplasty. Only 48 (13.8%) patients had simultaneous bilateral total knee arthroplasty. Their mean length of stays was 11.02 days. Venous thromboembolism was present in eight patients (2.3%), either with symptomatic deep vein thrombosis (1.4%) or with pulmonary embolism (1.1%). One hundred twenty-five (35.9%) patients had diabetes, and six of them had developed venous thromboembolism ( $P$ -value: 0.020). The mean post-op mobilization ( $4.63 \pm 3.5$  days) was higher in cases with venous thromboembolism ( $P$ -value: 0.045). Factors, such as the patients' age, history of venous thromboembolism, gender, history of cerebrovascular, obesity, operation time, and use of preoperative venous thromboembolism prophylaxis, showed no statistical significance with the incidence of venous thromboembolism in them. The result of our study are comparable to those reported in literature. *Diabetes mellitus* and delayed postoperative mobilization were the significant risk factors to the incidence of venous thromboembolism.

## Keywords

Total knee arthroplasty; Deep venous thrombosis; Pulmonary embolism; Thromboembolic events

## Introduction

Total knee arthroplasty (TKA) is a successful and a major orthopedic procedure for end stage knee osteoarthritis, which has a particularly high

risk in developing venous thromboembolism (VTE). The administration of thromboprophylaxis has been recommended routinely for years for such surgery<sup>[1,2]</sup>. Without prophylaxis, the rate of VTE in patients

undergoing TKA was reported to be between 40 and 60%, although the majority of these VTEs were asymptomatic<sup>[3]</sup>. This incidence was decreased significantly to 1.09% with the use of a VTE prophylaxis<sup>[4]</sup>. The etiology of VTE after a TKA is multifactorial, where obesity, *diabetes mellitus* (DM), age, gender, bilateral surgery, surgery time of more than two hours, history of DVT, and other factors were considered VTE risk factors of TKA<sup>[5-10]</sup>. In the entire country, a limited number of recent studies on VTE incidence following a TKA on the local population had been conducted<sup>[11]</sup>. The purpose of this study is to present the incidence and the risk factors of VTE post-TKA in our local patients.

### Methods

This retrospective study was conducted in the King Abdulaziz University Hospital in Jeddah, Saudi Arabia from January 2008 to December 2012. A total of 276 patients, who underwent 348 TKAs, were included in this study. Five files of these patients were not retrievable. The female patients accounted for 257 (73.9%) cases, and the males comprised 91 (26.1%) cases, with the patients' mean age at 64.41 years ( $\pm 9.30$ ). The patients had undergone revision TKAs, but those who went through a conversion of the unicondylar knee arthroplasty to TKA were excluded. Demographic, clinical, and radiological data were collected from the patients' medical records. The data that were used in this study included those from the patients with known VTE risk factors, postoperative mobilization, VTE prophylaxis, intensive care unit (ICU) admission, readmission for VTE, deep vein thrombosis (DVT) or pulmonary embolism (PE), and death. Venous thromboembolism occurs in cases with clinically diagnosed symptomatic DVT or PE. Positive DVT was only considered, if it was confirmed by Doppler ultrasound. Chest computed tomography (CT) angiography was the method used for the diagnosis of PE.

Statistical analysis on the patients' data was performed using IBM SPSS, version 22 (IBM Corp., Armonk, NY USA). Descriptive statistics was used to define the characteristics of the study variables through counts and percentages of the categorical and nominal variables, while the continuous variables were presented by the mean and the standard deviations. The chi-squared test was used to establish the relationship between the categorical variables. The means were compared using the independent *t*-test.

These tests were done, assuming a normal distribution of the data. Otherwise, the Welch's *t*-test for the two-group means was used. The *P*-value  $< 0.05$  was used as the basis in rejecting or accepting the null hypothesis.

### Results

Three hundred forty eight patients were included in this study. Unilateral TKA was performed in 300 (86.2%) cases, and simultaneous bilateral TKA was done in 48 (13.8%) cases. Fifteen patients had staged bilateral TKA in the same admission. The female patients accounted for 257 (73.9%) cases, and the male patients comprised 91 (26.1%) cases. The mean age of the patients was 64.41 ( $\pm 9.3$ ) years. Three hundred forty one (98.0%) patients had osteoarthritis, and seven (2.0%) patients had rheumatoid arthritis. The mean body mass index (BMI) of the 318 patients was 35.15 ( $\pm 6.6$ ), while that of 30 patients was not documented. The mean length of stay of all patients was 11.02 ( $\pm 6.2$ ) days. Eleven (3.2%) patients were reported to have post-op ICU admissions. One post-operative patient died due to myocardial infarction.

Eight (2.3%) patients had VTE postoperative, five (1.4%) patients had DVT, four (1.1%) patients had PE, and one patient had both DVT and PE. The diagnosis of either DVT or PE was done in the following postoperative days: 4, 7, 9, 12, 30, 82, and 229. Five (1.4%) VTE cases were diagnosed as inpatients, but another three (0.9%) cases were diagnosed after their discharge and were readmitted. Age, gender, and BMI were found to have no significant relationship with VTE development post TKA (*P*-value of  $< 0.05$ ). Two (4.2%) of the patients, who had simultaneous bilateral TKA developed VTE, and six (2.0%) of the unilateral group developed VTE, although these were found to be not statistically significant. The length of stay of the patients was affected significantly by the presence of VTE (*P*-value of 0.006). Patients, who had VTE, had a mean length of stay at 17.00 ( $\pm 5.68$ ) days, in comparison with the length of stay of the negative patients at 10.88 ( $\pm 5.62$ ) days. *Diabetes mellitus* was found in 125 (35.9%) cases. Six (4.8%) patients with VTE had DM (*P*-value of 0.020) (Table 1).

Aspirin was given as a preoperative treatment in 67 (19.3%) patients, but it showed no relationship with the development of VTE. Two (0.6%) patients did not receive a VTE prophylaxis neither prior nor after their operation, and another two did not receive postoperative prophylaxis. Preoperative VTE

**Table 1. Related risk factors in the incidence of venous thromboembolism and their significance.**

Factor		Total	Venous Thromboembolism		P-value
			Yes	No	
Total N (%)		348	8 (2.3%)	340 (97.7%)	N/A
Age (Mean ± SD)		64.41 ± 9.3	64.62 ± 9.0	64.41 ± 9.4	0.948
BMI (Mean ± SD)		35.15 ± 6.6	36.77 ± 9.0	35.10 ± 6.6	0.484
Gender	Male, N (%)	91	1 (1.1%)	90 (98.9%)	0.374
	Female, N (%)	257	7 (2.7%)	250 (97.3%)	
Smoking	No, N (%)	321	8 (2.5%)	313 (97.5%)	0.407
	Yes, N (%)	27	0 (0%)	27 (100.0%)	
Body Mass Index	Normal Weight, N (%)	12	1 (8.3%)	11 (91.7%)	0.535
	Overweight, N (%)	53	0 (0%)	53 (100.0%)	
	Class I Obesity, N (%)	99	3 (3.0%)	96 (97.0%)	
	Class II Obesity, N (%)	79	2 (2.5%)	77 (97.5%)	
Side of Operation	Bilateral, N (%)	48	2 (4.2%)	46 (95.8%)	0.352
	Unilateral, N (%)	300	6 (2.0%)	294 (98.0%)	
Previous history of DVT	No, N (%)	338	7 (2.1%)	331 (97.9%)	0.099
	Yes, N (%)	10	1 (10.0%)	9 (90.0%)	
Coronary Artery Disease	No, N (%)	324	8 (2.5%)	316 (97.5%)	0.436
	Yes, N (%)	24	0 (0%)	24 (100.0%)	
Heart Failure	No, N (%)	345	8 (2.3%)	337 (97.7%)	0.790
	Yes, N (%)	3	0 (0%)	3 (100.0%)	
Autoimmune Disease	No, N (%)	338	8 (2.4%)	330 (97.6%)	0.623
	Yes, N (%)	10	0 (0%)	10 (100.0%)	
Hypertension	No, N (%)	107	2 (1.9%)	105 (98.1%)	0.722
	Yes, N (%)	241	6 (2.5%)	235 (97.5%)	
Cerebrovascular Accident	No, N (%)	338	8 (2.4%)	330 (97.6%)	0.623
	Yes, N (%)	10	0 (0%)	10 (100.0%)	
Diabetes Mellitus	No, N (%)	223	2 (0.9%)	221 (99.1%)	0.020 <sup>a</sup>
	Yes, N (%)	125	6 (4.8%)	119 (95.2%)	
Pulmonary Disease	No, N (%)	313	8 (2.6%)	305 (97.4%)	0.339
	Yes, N (%)	35	0 (0%)	35 (100.0%)	
Dyslipidemia	No, N (%)	268	5 (1.9%)	263 (98.1%)	0.324
	Yes, N (%)	80	3 (3.8%)	77 (96.3%)	

<sup>a</sup>significant, using chi-squared test at <0.05 level

BMI: Body Mass Index; SD: standard deviation; DVT: deep vein thrombosis

**Table 2. Venous thromboembolism prophylaxis, length of stay, and start of mobilization.**

Medication		Total	Venous Thromboembolism		P-value
			Yes	No	
Total, N (%)		348	8 (2.3%)	340 (97.7%)	N/A
Regular use of aspirin preop	No, N (%)	281	6 (2.1%)	275 (97.9%)	0.677
	Yes, N (%)	67	2 (3.0%)	65 (97.0%)	
Use of VTE prophylaxis	No, N (%)	2	0 (0%)	2 (100.0%)	0.828
	Yes, N (%)	346	8 (2.3%)	338 (97.7%)	
Use of preop VTE prophylaxis	No, N (%)	192	6 (3.1%)	186 (96.9%)	0.258
	Yes, N (%)	155	2 (1.3%)	153 (98.7%)	
Use of postop VTE prophylaxis	No, N (%)	4	0 (0%)	4 (100.0%)	0.757
	Yes, N (%)	343	8 (2.3%)	335 (97.7%)	
Length of stay (days)	Mean ± SD	11.02 ± 6.2	17.00 ± 5.68	10.88 ± 5.62	0.006 <sup>a</sup>
Mobilization day postop	Mean ± SD	3.06 ± 2.2	4.63 ± 3.5	3.02 ± 2.2	0.045 <sup>a</sup>
ICU admission postop	No, N (%)	337	7 (2.1%)	330 (97.9%)	0.127
	Yes, N (%)	11	1 (9.1%)	10 (90.9%)	

<sup>a</sup>significant using Welch's t-test at <0.05 level

VTE: Venous Thromboembolism; ICU: Intensive Care Unit; preop: preoperative; postop: postoperative

prophylaxis was given to 155 (44.7%) patients, two of whom had VTE. One hundred ninety two (55.3%) patients did not receive pre-op VTE prophylaxis, and only six cases of them had VTE. This difference produced no statistical significance ( $P$ -value of 0.258). The beginning of the mean postop mobilization day was longer in patients, who later developed VTE, from 3.02 ( $\pm$  2.2) to 4.63 ( $\pm$  3.5) days, which was statistically significant ( $P$ -value of 0.045) (Table 2).

## Discussion

The rate of incidence of *symptomatic* VTE after knee arthroplasty as reported in a previous work was within the range of 2%–3%<sup>[7]</sup>. The rate of incidence in our study was 2.3%, which includes the DVT incidence at 1.4% and that of PE at 1.1%. These rates are almost similar to the findings of previous studies, such those of Januel *et al.*<sup>[4]</sup>, White *et al.*<sup>[7]</sup>, Almegren *et al.*<sup>[11]</sup> and Bakhsh<sup>[12]</sup> sampled between May 1989 and August 2005 the same population of 205 patients and reported a rate of incidence of 2.4%. The incidence of VTE among the inpatients in our study was 1.4%. This is comparative to what was reported by Januel *et al.*<sup>[4]</sup>, which was 1.9% for the symptomatic postop VTE before hospital discharge. Their study involved the meta-analysis of 47 randomized clinical trials and observational studies that included 44,844 cases, who received prophylaxis for total or partial knee arthroplasty and with pooled rates of symptomatic DVT of 0.63% and 0.27% for PE.

A number of risk factors for the development of VTE were identified from previous works<sup>[5-10]</sup>. *Diabetes mellitus* is generally considered to be an increased risk for VTE<sup>[13,14]</sup>, although in most studies, it was not proven to be a risk factor for VTE in TKA patients<sup>[5,8,15]</sup>. It was even associated with lower risk<sup>[16]</sup>. In this study, DM was found to be a risk factor for VTE in TKA patients. The risk factors associated with venous stasis had increased the risk of VTE after TKA. Conversely, the early mobilization of patients after their surgery had been shown to decrease the relative risk of VTE. The American Academy of Orthopedic Surgeons (AAOS) recommended to administer early mobilization as soon as possible following a TKA<sup>[2,7]</sup>. In this study, a delayed post-op mobilization was significantly associated with VTE, which is also consistent with the results of other studies<sup>[7,13-15]</sup>. Based on the AAOS VTE prevention guidelines, the current evidence is not clear about whether factors other than the history of previous VTE can increase or decrease the risk of VTE in patients undergoing elective TKA<sup>[2]</sup>. This factor had

no significance with the increased rate of incidence of VTE in our study. Simultaneous bilateral TKA did not have a significant impact as a risk for VTE over the unilateral TKA in our study, but in some literature, it showed an increased risk to VTE<sup>[6,16]</sup>. Other factors, such as having advanced age, female gender, history of cerebrovascular event, heart failure, obesity, and longer operation time, were associated with more VTE post TKA, as suggested in some studies<sup>[5,7,8,15,19-23]</sup>, but these findings are not consistent with those in our study.

Patients undergoing TKR are at risk to develop VTE disease. There is a general agreement that these patients require prophylaxis<sup>[24]</sup>. Nearly all (99.4%) of our patients were given aspirin as a pharmacological prophylaxis for their VTE, which was recommended by the AAOS guideline to decrease the incidence of such events<sup>[2]</sup>. The AAOS guideline panel was unable to recommend for or against a specific prophylaxis regimen, because current sets of evidence are still unclear about which prophylaxis has the optimal or the suboptimal impact. In this study, the regular use of aspirin or the use of a preoperative pharmacological prophylaxis had no statistical significance in the prevention of VTE. Also, the length of stay of the patients was significantly affected by the VTE in this study.

This study had several limitations, such as those brought about by the missing files and data, incorrect recording, and incomplete data, which are related to the retrospective nature of the study. Asymptomatic VTE could not be traced in this type of study. Also, the number of cases is considered relatively low. We recommend the conduct of further studies with a greater number of cases and with randomized clinical trials of the prophylaxis for VTE and other complications post TKA, particularly on our local population due to the deficiency of this kind of studies in this field.

## Conclusions

This study showed that the incidence of VTE post primary TKA in our sample population is comparable to the findings reported in literature. History of DM and delayed post-op mobilization of the patients were found to be associated with an increased risk of post-operative VTE after TKA.

## Conflict of Interest

The authors declares that they have no conflict of interest that is related to this study and this article.

## Disclosure

The authors did not receive any type of commercial support either in the form of compensation or financial support for this case report. The authors have no financial interest in any of the products, devices, or drugs mentioned in this article.

## Ethical Approval

The study was approved by the Ethics Committee of the KAUH in Jeddah, Kingdom of Saudi Arabia, also known as the Institutional Review Board of Hospitals.

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## نسبة حدوث الجلطات الدموية بعد عمليات المفصل الصناعي للركبة والعوامل المصاحبة

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**المستخلص.** المرضى الذين يخضعون لعملية مفصل الركبة الصناعي الكلي معرضون لخطر الإصابة بالجلطات الدموية الوريدية ولها اسباب متعددة، والغرض من هذه الدراسة عرض نسبة حدوث الجلطات الدموية الوريدية بعد عملية مفصل الركبة الصناعي الكلي والعوامل المرتبطة بها في مجتمعنا، وقد اجرينا دراسة استرجاعية لـ ٣٤٨ عملية مفصل ركبة صناعي تمت بين يناير ٢٠٠٨ وديسمبر ٢٠١٢، في مستشفى جامعة الملك عبد العزيز وكان منها ٣٠٠ عملية (٨٦٪) في جانب واحد و ٤٨ أخرى (١٣,٨٪) في كلا الجانبين ومتزامنين، و كان متوسط مدة الإقامة ١١,٢ يوما (٦,٣ ±) الانحراف المعياري.

الانسداد الرئوي (١,١٪) و (١,٤٪) تجلط الاوردة العميقة منها (٢,٣٪)، اعراض الجلطات الدموية الوريدية كانت موجودة في ٨ حالات

تم العثور على مرض السكري في ١٢٥ حالة (٣٥,٩٪) و ٦ حالات جلطات وريدية دموية قيمة (٠,٢٠) ( $p = ٠,٠٤٥$ )

الجلطات الدموية الوريدي متوسط بداية اول يوم للحركة بعد العملية (٣,٥ ± ٤,٦٣) وكانت أعلى في حالات قيمة (٠,٠٤٥) ( $p = ٠,٠٤٥$ ) وعوامل أخرى مثل التقدم في العمر، والتاريخ السابق للجلطات، والجنس الأنثوي، والسمنة، والزمن الذي استغرقتة العملية، واستخدام العلاج الوقائي من الجلطات الوريدية قبل العملية لم تكن لها أي أهمية إحصائية

اظهرت الدراسة ان نسبة حدوث الجلطات الدموية الوريدية بعد عملية مفصل الركبة الصناعي الكلي في مجتمعنا مماثلة لتلك في الدراسات الأخرى، كما أن الإصابة بمرض السكري، والتأخر في الحركة من العوامل المؤثرة في حدوث الجلطات الدموية الوريدية.